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CENTRAL FAX CENTERApplication No. 09/914,006
After Final Office Action of March 25, 2008

JUN 25 2008

Docket No.: 05899-00013-US

REMARKS

The Office Action mailed March 25, 2008 has been carefully considered and the following response prepared. Claims 14-18, 20-26, 29-37, 40 and 41 are pending in the application.

Nonstatutory Obviousness-type Double Patenting Rejection

At page 2 of the Office Action, the Examiner maintained the rejection of claims 14-18, 20-26, 29-37, 40, and 41 on the ground of nonstatutory obviousness-type double patenting over claims 1-25 of U.S. patent No. 6,177,264 (the '264 patent). The Examiner alleged that, although the instant claims and the patented claims are not identical, they are not patentably distinct from the claims of the '264 patent because the claimed transformed microorganism and claimed methods for production of L-valine of the present application are obvious variations over the patent claims to the isolated polynucleotides from *Corynebacterium* encoding panB, panC, and ilvBNCD and methods using microorganisms comprising such polynucleotides.

The Examiner alleged that Examples 1-8 of the '264 patent provide support for the patent claims and disclose cloning and expression of panB, panC, ilvBN, ilvC and ilvD genes, construction of inactivated panC and ilvA mutations and culturing of *Corynebacterium* strains having these mutations. The Examiner referred to column 7, line 5 to column 14, line 26 of the '264 patent, which corresponds to Examples 1-8. The Examiner also pointed out that SEQ ID NO: 1 of the present application and SEQ ID NO: 4 of the '264 patent show 100 % sequence identity. *In re Vogel*, 164 USPQ 619 (CCPA 1970) was cited in support of the use of the specification to determine whether a claim in the application defines an obvious variation of an invention claimed in the patent. The Examiner concluded that the disclosures of the '264 patent support claims 1-25 for the isolated polynucleotides from *Corynebacterium* encoding panB, panC, ilvD and ilvBNCD.

Applicants again traverse this rejection.

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In determining whether a nonstatutory basis exists for a double patenting rejection, the claims of the application and the claims of the patent are compared to determine whether the claims of the application are merely an obvious variation of an invention claimed in the patent. Moreover, when considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle GmbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). According to *In re Vogel* the prohibition on using the disclosure of the patent as prior art does not mean it may not be used at all. In certain circumstances it may be used as a dictionary to learn the meaning of terms in a claim. It may also be used as required to answer the question of what is or is not an obvious variation of a claim. On this point *In re Vogel* states:

We recognize that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim. A claim is a group of words defining only the boundary of the patent monopoly. It may not describe any physical thing and indeed may encompass physical things not yet dreamed of. How can it be obvious or not obvious to modify a legal boundary? The disclosure, however, sets forth at least one tangible embodiment within the claim, and it is less difficult and more meaningful to judge whether that thing has been modified in an obvious manner. It must be noted that this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined. *Id.*, at 622.

In re Vogel allows the comparison of a tangible embodiment of the claimed invention disclosed in the patent to be compared to the claims of the application to judge whether the thing has been modified in an obvious manner. *In re Vogel* does not sanction the wholesale use of the disclosure of the patent under the guise that it pertains to the claimed invention. Such an interpretation would render meaningless the prohibition on using the disclosure of the patent as prior art, as most of the disclosure in a patent pertains to the claimed invention in some manner.

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Claims 1-11 of the '264 patent are directed to isolated polynucleotides from *Corynebacterium* encoding the panB gene product or panC gene product, or both, vectors comprising the polynucleotides, and microorganisms comprising the vectors. There appears to be an error in claim 1 relating to the sequence identifiers for ketopantoate hydroxymethyl-transferase (panC) and pantothenate synthetase (panC). Example 1, at column 7, lines 59-66 indicate that the nucleotide sequence encoding panB and panC are found in SEQ ID NO: 1. SEQ ID NO: 1 contains an open reading frame 813 base pairs in length, identified as panB, which codes for a polypeptide of 271 amino acids and is set out in SEQ ID NO: 2. The second open reading frame, identified as panC, comprises 837 base pairs, and codes for a polypeptide of 279 amino acids, which is described as SEQ ID NO: 3. SEQ ID NO: 4 refers to the nucleotide sequence of dihydroxy acid dehydratase (ilvD), as indicated at column 9, lines 63-64. When the correct sequence identifiers are used in the claims, or the claims are construed using the names of the enzymes, it is apparent that Example 1, to the extent represented by the actual sequences of SEQ ID NO: 2 and SEQ ID NO: 3 shown in the Sequence Listing, appears to disclose an embodiment of claims 1-8 and 10. Claim 9 appears to be indefinite due to an error in the identification of the vector. Example 4 discloses the microorganisms ATCC13032/pEKEx2panBC and ATCC13032 Δ ilvA/pEKEx2panBC that appear to be embodiments of claims 10 and 11.

Claims 12-20, 24 and 25 (in part) of the '264 patent are directed to methods for producing pantothenic acid. Claim 12, the only independent claim, requires the steps of transforming a vector comprising a panB gene and a panC gene into a microorganism, growing the recombinant microorganism under conditions suitable for production of pantothenic acid in an appropriate culture medium and recovering pantothenic acid from the culture medium. Examples 7 and 8 in conjunction with Example 4 appear to disclose embodiments of claim 12, except that the step of recovering the pantothenate from the culture medium is not explicitly disclosed. Example 7 in conjunction with Example 4 discloses preparation of the transformed *C. glutamicum* strains ATCC13032/pEKEx2panBC and ATCC13032 Δ ilvA/pEKEx2panBC, and culturing of the cells in medium to produce pantothenate. Example 8 in conjunction with

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Example 4 discloses the preparation of the transformed *C. glutamicum* strain ATCC13032 Δ ilvA/pECM3ilvBNCD pEKEx2panBC, and culturing of the cells in medium with added β -alanine to produce pantothenate.

Claims 21-23 of the '264 patent are also directed to methods of producing pantothenic acid. Claims 21 and 22 require inserting an expression cassette upstream from the panB and panC genes in *Corynebacterium*. Claim 23 requires the step of increasing the stability of the mRNA which is translated from the panB and panC genes and/or the step of preventing the degradation of the panB and panC gene products. There do not appear to be any embodiments of these claims in the examples.

Examples 2, 3, 5 and 6, relating to cloning and sequencing of the ilvD gene, construction of an ilvA deletion mutant from *C. glutamicum*, construction of a panC mutant of *C. glutamicum* and use for quantitative determination of D-pantothenate, do not appear to disclose any embodiments of the inventions claimed in claims 1-25.

The portion of the specification that can be used in the double patenting analysis is thus limited to the aforementioned specific disclosures in Examples 1 and 4, and, possibly Examples 7 and 8. Although the examples of the '264 patent disclose materials such as the ilvD, ilvBN, and ilvC genes, an ilvA deletion mutant of *C. glutamicum* and an inactivated panC mutant of *C. glutamicum*, that may also be used with some of the microorganisms and methods of the present application, they are not claimed nor do they represent tangible embodiments of the claimed invention. The remaining portions of Examples 1, 4, 7 and 8, and Examples 2, 3, 5 and 6 therefore cannot be used in the double patenting analysis because to do so would be impermissibly using them as prior art against the present claims.

Claims 14-17 and 41 of the present application are directed to a microorganism transformed with a nucleotide sequence encoding dihydroxy acid dehydratase (ilvD), nucleotide sequences encoding acetohydroxy acid synthase and isomeroreductase (ilvBNC) or both ilvD and ilvBNC, in which microorganism the activity of one or more enzymes that are specifically involved in the synthesis of D-pantothenate is reduced or eliminated, wherein the one or more

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enzymes are selected from the group consisting of ketopantoate hydroxymethyl transferase (panB), pantothenate ligase (panC), ketopantoic acid reductase (panE) and aspartate decarboxylase (panD) and the activity of the one or more enzymes is reduced or eliminated as a result of deletion of all or a part of the nucleotide sequence encoding the enzyme in the microorganism, and wherein the microorganism is a *Corynebacterium* species and the nucleotide sequence encoding ilvD comprises the portion of SEQ ID NO: 1 encoding ilvD.

Claims 10 and 11 of the '264 patent, which are directed to microorganisms, require a vector comprising a nucleotide sequence encoding panB or panC. (The transformed microorganisms used in the methods of claims 12-20, 24 and 25 require transformation with a vector comprising a nucleotide sequence encoding panB and panC.)

The microorganisms of claims 14-17 and 41 are not identical to the microorganisms of claim 10 or 11 of the '264 patent. Additionally, claims 14-17 and 41 are not obvious variations of claims 10 and 11 because there is no equivalent to the vector comprising a nucleotide sequence encoding panB or panC. The microorganisms of claims 10 and 11 of the '264 patent contain at least one nucleotide sequence encoding panB or panC in addition to the native sequence(s). By contrast, the transformed microorganisms of claims 14-17 and 41 contain only native panB and/or panC sequences, or the native panB and/or panC sequences have been partially or completely deleted.

Claims 18, 20-26, 29-37 and 40 of the present application are not identical to the methods of claims 12-25 of the '264 patent. Claims 18, 20-26, 29-37 and 40 are directed to methods of producing L-valine. Claims 12-25 of the '264 patent, however, are directed to methods for producing pantothenate, a different substance. Additionally, claims 18, 20-26, 29-37 and 40 are not obvious variations of claims 12-15 of the '264 patent. Pantothenate and L-valine have very different structures, and methods of preparing one could not in any way be considered the equivalent or suggestive of the other.

When the correct standard is applied in the instant rejection, it is clear that claims 14-18, 20-26, 29-37, 40, and 41 are not obvious variations of claims 1-25 of the '264 patent. Claims 14-

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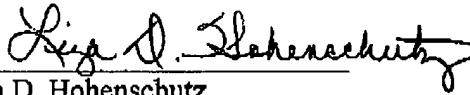
18, 20-26, 29-37, 40, and 41 are patentably distinct from claims 1-25 of the '264 patent.
Withdrawal of this double patenting rejection is again respectfully requested.

In view of the above, the present application is believed to be in a condition for allowance. Reconsideration of the application is requested and an early Notice of Allowance is earnestly solicited.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 03-2775, under Order No. 05899-00013-US from which the undersigned is authorized to draw.

Dated: June 25, 2008

Respectfully submitted,

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